Attorney Docket No. P67065US0 National Stage of PCT/EP03/14654

Amendments to the claims:

JC17 Rec'd PCT/PTO 17 JUN 2005

This listing of claims replaces all prior versions, and listings, of claims in the application.

Listing of claims:

1 (original): Peptides with biological activity against infection by HIV, having the amino acid sequence

$$Z_1$$
-LE- X_1 -IP- X_2 - X_3 - X_4 -P- X_5 - X_6 - X_7 - X_8 - X_9 - X_{10} -K- X_{11} - X_{12} - X_{13} - X_{14} - X_{15} - Z_2 ,

wherein

 X_1 is a lysine, alanine, or aspartic acid;

 X_2 is a cysteine, methionine or isoleucine;

 X_3 is a serine, cysteine, lysine or glycine;

 X_4 is an isoleucine, alanine, phenylalanine or cysteine;

X₅ is a proline, D-proline or a substituted L-or D-proline;

X₆ is a cysteine or glutamic acid;

 X_7 is an amino acid with a hydrophobic or an aromatic side chain or cysteine;

X₈ is an amino acid with a hydrophobic or an aromatic side chain or cysteine;

X₉ is an amino acid with an aromatic side chain;

 X_{10} is a glycine, alanine or asparagine;

X₁₁ is a proline, aspartic acid, octahydroindolyl-2-carboxylic acid or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

X₁₂ is a phenylalanine, alanine, glycine, glutamic acid or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

X₁₃ is an amino acid with a hydrophobic or an aromatic side chain;

 X_{14} is an amino acid with a hydrophobic or an aromatic side chain;

 X_{15} is a phenylalanine or deletion;

Z₁ is NH₂ or a sequence of 1 to 10 amino acid residues;

Z₂ is COOH or a sequence of 1 to 10 amino acid residues;

and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof;

and with the provisio that

- (a) if X_{12} is alanine, glycine, glutamic acid, or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid than X_{13} , X_{14} and X_{15} are phenylalanine, valine and phenylalanine respectively; and/or
- (b) if X_{12} is phenylalanine, than X_{13} , X_{14} and X_{15} are valine, phenylalanine and a deletion, respectively; and
- (c) that there are at maximum two cysteine residues in a peptide.

2 (original): Peptides according to claim 1 with a biological activity against infection by HIV having the amino acid sequence

$$Z_1$$
-LE- X_1 -IP- X_2 - X_3 - X_4 -P- X_5 - X_6 - X_7 - X_8 - X_9 - X_{10} -K- X_{11} -FVF- Z_2 ,

wherein

 X_1 is a lysine, alanine or aspartic acid;

 X_2 is a cysteine, methionine or isoleucine;

X₃ is a serine, cysteine or glycine;

X₄ is a isoleucine or cysteine;

X₅ is a proline, D-proline or any substituted L- or D-proline;

 X_6 is a cysteine or glutamic acid;

 X_7 is a phenylalanine, cysteine, valine, isoleucine or 3,3-diphenylalanine;

X₈ is a phenylalanine, leucine, alanine, glycine, cysteine, D-1,2,3,4-tetrahydroisoquino-

line-3-carboxylic acid or L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid;

 X_9 is an amino acid with an aromatic side chain;

 X_{10} is a glycine or asparagine;

 X_{11} is a proline or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic;

 Z_1 is NH₂ or a sequence of 1 to 10 amino acid residues;

Z₂ is COOH or a sequence of 1 to 10 amino acid residues;

and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof,

with the provisio that

- (a) if two cysteine residues are present, said residues are separated by four other amino acid residues; and
- (b) L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid (L-Tic), D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (D-Tic) and/or 3,3-diphenylalanine are present, no cysteine residue is present.
- 3 (currently amended): Peptides according to elaims 1 to 2 claim 1 with a biological activity against infection by HIV, having the amino acid sequence

$$Z_1$$
-LE- X_1 -IP- X_2 - X_3 -IP- X_5 - X_6 - X_7 - X_8 -F- X_{10} -KPFVF- Z_2 , wherein

 X_1 is a lysine, alanine or aspartic acid;

 X_2 is a cysteine, methionine or isoleucine;

X₃ is a serine or glycine;

X₅ is a L-proline, D-proline or any substituted L- or D-proline

X₆ is a cysteine or glutamic acid;

 X_7 is a phenyalalnine or valine;

X₈ is a phenylalanine, leucine, alanine or L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid;

X₁₀ is a glycine or asparagine;

 Z_1 is NH_2 or a sequence of 1 to 10 amino acid residues;

Z₂ is COOH or a sequence of 1 to 10 amino acid residues, and

and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof.

4 (currently amended): Peptides according to claim 1 to 3, having the amino acid sequence Z₁-LEAIP-X₂-SIP-X₅-X₆-V-X₈-FNKPFVF-Z₂,

wherein

X₂ and X₆ are cysteines, or X₂ is methionine and X₆ is glutamic acid

X₅ is a D-proline or L-proline;

X₈ is an amino acid with a hydrophobic or an aromatic side chain or lysine;

 Z_1 is NH_2 or a sequence of 1 to 10 amino acid residues;

 Z_2 is COOH or a sequence of 1 to 10 amino acid residues;

and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or

Attorney Docket No. P67065US0 National Stage of PCT/EP03/14654

glycosylated derivatives, and mutants thereof, with biological activity against infection by

HIV,

with the proviso that at least one of the following is true:

X₅ is D-proline or

X₈ is not lysine or

 X_2 and X_6 are cysteine.

5 (currently amended): Peptides according to anyone of the claim 1 to 4, wherein the cysteine

residues at positions 6 and 11, 6 and 12, 7 and 12, or 8 and 13 are connected by an

intramolecular disulfide bond.

6 (currently amended): Peptides according to anyone of the claim 1 to 4, with a single cysteine

residue, wherein said cysteine residue is connected by an intermolecular disulfide bond to

another peptide with a single cysteine residue, forming a homo-dimer.

7 (currently amended): Peptides according to anyone of the claims 1 to 6 claim 1, wherein the

leucine residue at amino acid position 1 and the glutamic acid at amino acid position 2 are

covalently linked by an N-alkylated amide bond or by an ester bond or by a reduced peptide

bond or by a retro-inverso peptide bond or by an N-alkylated retro-inverso peptide bond.

8

8 (currently amended): Peptides according to any of the claims 1 to 7 claim 1 with one of the amino acid sequences

VIR-121	LEAIPMSIPpEVAFNKPFVF	SEQ ID NO. 2
VIR-161	LEAIPCSIPpCVAFNKPFVF	SEQ ID NO. 3
VIR-162	LEAIPCSIPPCVGFGKPFVF	SEQ ID NO. 4
VIR-163	LEAIPCSIPPCVLFNKPFVF	SEQ ID NO. 5
VIR-164	LEAIPCSIPPCVFFNKPFVF	SEQ ID NO. 6
VIR-165	LEAIPCSIPPCFAFNKPFVF	SEQ ID NO. 7
VIR-166	LEAIPCSIPPCVA(D-Tic)NKP(D-Tic)FVF	SEQ ID NO. 8
VIR-170	LEAIPMSIPPEVFFGKPFVF	SEQ ID NO. 9
VIR-175	LEAIPMSIPPEFLFGKPFVF	SEQ ID NO. 10
VIR-182	LEAIPMSIPPELAFAKPFVF	SEQ ID NO. 11
VIR-184	LEAIPMSIPPEIAFNKPFVF	SEQ ID NO. 12
VIR-190	LEAIPMSIPpEVGFGKPFVF	SEQ ID NO. 13
VIR-191	LEAIPMSIPpEVLFGKPFVF	SEQ ID NO. 14
VIR-192	LEAIPMSIPpEVFFGKPFVF	SEQ ID NO. 15
VIR-193	LEAIPMSIPpEFAFNKPFVF	SEQ ID NO. 16
VIR-197	LEAIPMSIPpEVFFNKPFVF	SEQ ID NO. 17
VIR-199	LEAIPMSIPpEFLFNKPFVF	SEQ ID NO. 18

Attorney Docket No. P67065US0 National Stage of PCT/EP03/14654

VIR-229	LEAIPISIPpEVAFNKPFVF	SEQ ID NO. 19
VIR-234	LEAIPMGIPpEVAFNKPFVF	SEQ ID NO. 20
VIR-243	LEAIPMSIPPEFAFNKDFVF	SEQ ID NO. 21
VIR-252	LEDIPMSIPpEVAFNKPFVF	SEQ ID NO. 22
VIR-255	LEKIPMSIPpEVAFNKPFVF	SEQ ID NO. 23
VIR-257	LEAIPMSIPpEV(cyclohexylalanine)FNKPFVF	SEQ ID NO. 24
VIR-258	LEAIPMSIPpE(1-naphthylalanine)AFNKPFVF	SEQ ID NO. 25
VIR-259	LEAIPMSIPpE(p-fluorophenylanine)AFNKPFVF	SEQ ID NO. 26
VIR-260	LEAIPMSIPpEV(4-pyridylalanine)FNKPFVF	SEQ ID NO. 27
VIR-261	LEAIPMSIPpE(3,3-diphenylalanine)AFNKPFVF	SEQ ID NO. 28
VIR-262	LEAIPMSIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 29
VIR-263	LEAIPMSIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 30
VIR-264	LEAIPMSIPpEV(3-benzothienylalanine)FNKPFVF	SEQ ID NO. 31
VIR-265	LEAIPMSIPpEV(3-thienylalanine)FNKPFVF	SEQ ID NO. 32
VIR-266	LEAIPMSIPpEVWFNKPFVF	SEQ ID NO. 33
VIR-268	LEAIPMSIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 34
VIR-269	LEAIPMSIPpEVAFNK(Oic)FVF	SEQ ID NO. 35
VIR-272	LEAIPMCIPPECLFNKPFVF	SEQ ID NO. 36
VIR-273	LEAIPMCIPPECFFNKPFVF	SEQ ID NO. 37
VIR-274	LEAIPMCIPPECLFGKPFVF	SEQ ID NO. 38

Attorney Docket No. P67065US0 National Stage of PCT/EP03/14654

VIR-280	LEAIPCSIPPCFLFGKPFVF	SEQ ID NO. 39
VIR-284	LEAIPISIPPEVFFGKPFVF	SEQ ID NO. 40
VIR-286	LEAIPISIPPELAFAKPFVF	SEQ ID NO. 41
VIR-290	LEAIPISIPpEVFFGKPFVF	SEQ ID NO. 42
VIR-298	LEAIPISIPpEVWFNKPFVF	SEQ ID NO. 43
VIR-320	LEAIPMGIPpEVFFGKPFVF	SEQ ID NO. 44
VIR-322	LEAIPMGIPpEVFFNKPFVF	SEQ ID NO. 45
VIR-323	LEAIPMGIPpEFLFNKPFVF	SEQ ID NO. 46
VIR-326	LEDIPMGIPpEVAFNKPFVF	SEQ ID NO. 47
VIR-328	LEAIPMGIPpEVWFNKPFVF	SEQ ID NO. 48
VIR-344	LEAIPCSIPPCVFFGKPFVF	SEQ ID NO. 49
VIR-345	LEAIPCSIPPCFLFGKPFVF	SEQ ID NO. 50
VIR-346	LEAIPCSIPPCLAFAKPFVF	SEQ ID NO. 51
VIR-348	LEAIPCSIPpCVGFGKPFVF	SEQ ID NO. 52
VIR-350	LEAIPCSIPpCVFFGKPFVF	SEQ ID NO. 53
VIR-351	LEAIPCSIPpCFAFNKPFVF	SEQ ID NO. 54
VIR-352	LEAIPCSIPpCVFFNKPFVF	SEQ ID NO. 55
VIR-353	LEAIPCSIPpCFLFNKPFVF	SEQ ID NO. 56
VIR-354	LEAIPCSIPpCVAFNKPFVF	SEQ ID NO. 57
VIR-355	LEAIPCGIPpCVAFNKPFVF	SEQ ID NO. 58

Attorney Docket No. P67065US0 National Stage of PCT/EP03/14654

VIR-356	LEAIPCSIPPCFAFNKDFVF	SEQ ID NO. 59
VIR-357	LEDIPCSIPpCVAFNKPFVF	SEQ ID NO. 60
VIR-358	LEKIPCSIPpCVAFNKPFVF	SEQ ID NO. 61
VIR-376	LEAIPMSIPpEFLFGKPAFVF	SEQ ID NO. 62
VIR-377	LEAIPMSIPpEFLFGKPGFVF	SEQ ID NO. 63
VIR-380	LEAIPMSIPpEFLFGKPFFVF	SEQ ID NO. 64
VIR-384	LEAIPMSIPpEFLFGKPEFVF	SEQ ID NO. 65
VIR-396	LEAIPMSAPpEFLFGKPFVF	SEQ ID NO. 66
VIR-400	LEAIPMSFPpEFLFGKPFVF	SEQ ID NO. 67
VIR-416	LEAIPMGIPpEFLFGKPFVF	SEQ ID NO. 68
VIR-418	LEKIPMGIPpEFLFGKPFVF	SEQ ID NO. 69
VIR-445	LEAIPISIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 70
VIR-447	LEAIPISIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 71
VIR-448	LEAIPMGIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 72
VIR-449	LEAIPMGIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 73
VIR-452	LEDIPMSIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 74
VIR-454	LEKIPMSIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 75
VIR-455	LEKIPMSIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 76
VIR-479	LEDIPIGIPpEFLFNKPFVF	SEQ ID NO. 77
VIR-483	LEKIPIGIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 78

Attorney Docket No. P67065US0 National Stage of PCT/EP03/14654

VIR-484	LEKIPIGIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 79
VIR-485	LEKIPIGIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 80
VIR-487	LEDIPIGIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 81
VIR-488	LEDIPIGIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 82
VIR-512	<i>N-Me-</i> LEAIPMSIPPEFLFGKPFVF	SEQ ID NO. 83
VIR-568	LEAIPMSCPPEFCFGKPFVF	SEQ ID NO. 84
VIR-570	LEAIPCSIPPECLFGKPFVF	SEQ ID NO. 85
VIR-576	(LEAIPCSIPPEFLFGKPFVF) ₂	SEQ ID NO. 86
VIR-580	LEAIPMSIPPEFLFGKPFVF-miniPEG	SEQ ID NO. 87
VIR-590	LEAIPMKIPPEFLFGKPFVF	SEQ ID NO. 88.

- 9 (currently amended): The peptides according to anyone of claims 1 to 8 claim 1, which interact with the fusion peptide of HIV.
- 10 (currently amended): The peptides according to anyone of claims 1 to 9 claim 1, which have an IC₅₀ of equal or below 6500 nM, preferably those having an IC₅₀ of equal or below 2000 nM and most preferably those having an IC₅₀ of equal or below 800 nM such as VIR-344 (SEQ ID NO. 49) with an IC₅₀ of 348 nM, VIR-345 (SEQ ID NO. 50) with an IC₅₀ of 298 nM, VIR-353 (SEQ ID NO. 56) with an IC₅₀ of 225 nM, VIR-357 (SEQ ID NO. 60) with an IC₅₀ of 497 nM, VIR-358 (SEQ ID NO. 61) with an IC₅₀ of 706 nM, VIR-449 (SEQ ID NO. 73)

with an IC₅₀ of 274 nM, VIR-455 (SEQ ID NO. 76) with an IC₅₀ of 134 nM, VIR-484 (SEQ ID NO. 79) with an IC₅₀ of 100 nM, VIR-512 (SEQ ID NO. 83) with an IC₅₀ of 138 nM, VIR-576 (SEQ ID NO. 86) with an IC₅₀ of 107 nM and VIR-580 (SEQ ID NO. 87) with an IC₅₀ of 150 nM.

- 11 (currently amended): Nucleic acids coding for peptides according to any-of-claims 1 to 10 claim 1.
- 12 (currently amended): Antibodies binding specifically to peptides according to elaims 1 to 10 claim 1.
- 13 (currently amended): A medicament containing the peptides according to claims 1 to 10 claim

 1, nucleic acids of claim 11 coding for the peptides or antibodies of claim 12 binding specifically to the peptides.
- 14 (original): The medicament of claim 13 in galenic formulations for oral, intravenous, intramuscular, intracutaneous, subcutaneous, intrathecal administration, and as an aerosol for transpulmonary administration.

- 15 (currently amended): The medicament of claim 13 or 14 comprising at least one further therapeutic agent.
- 16 (original): The medicament of claim 15, wherein the said at least one further therapeutic agent is a viral protease inhibitor, a reverse transcriptase inhibitor, a fusion inhibitor, a cytokine, a cytokine inhibitor, a glycosylation inhibitor or a viral mRNA inhibitor.
- 17 (currently amended): Use of the peptides according to elaims 1 to 10 claim 1 for the manufacturing of a medicament for the treatment of HIV infections.
- 18 (currently amended): An assay for determining molecules capable of interaction with the fusion peptide of HIV, comprising a peptide according to anyone of claims 1 to 10 claim 1.
- 19 (currently amended): Use of the peptides according to anyone of claims 1 to 10 claim 1 in an assay according to claim 16 for determining molecules capable of interaction with the fusion peptide of HIV.
- 20 (currently amended): A diagnostic agent containing the peptides according to elaims 1 to 10 claim 1, nucleic acids of claim-11 coding for the peptides or antibodies of claim-12 binding specifically to the peptides.

21 (original): Use of the diagnostic agent according to claim 18 for assay systems for testing isolated plasma, tissue, urine and cerebrospinal fluid levels for HIV infection.